

seroprevalence for this age group was low. The performance of serial cross-sectional sero-surveillance substantially deteriorates if test specificity is not near 100% or pre-existing seroprevalence is not near zero. These potential limitations could be mitigated by choosing a higher titer cutoff for seropositivity. If the epidemic doubling time is longer than 6 d, then serial cross-sectional sero-surveillance with 300 specimens per week would yield reliable estimates when IAR reaches around 6%-10%.

Conclusions: Serial cross-sectional serologic data together with clinical surveillance data can allow reliable real-time estimates of IAR and severity in an emerging pandemic. Sero-surveillance for pandemics should be considered.

Ref. No.: PHE-20

P110-Ab0092

A Longitudinal Study of Infection Attack Rates among Hospital Outpatients in Hong Kong during the Epidemic of the Human Swine Influenza A/H1N1 Virus in 2009 by Tracking Temporal Changes in Age-specific Seroprevalence Rates

Joseph Wu¹, Kathy Leung¹, Ranawaka Perera¹, Daniel Chu¹, Cheuk Kwong Lee², Ivan Hung¹, Che Kit Lin², Su Vui Lo³, Yu Lung Lau¹, Gabriel Leung¹, Benjamin Cowling¹, Malik Peiris¹

¹The University of Hong Kong, Hong Kong, ²Red Cross Blood Transfusion Services, Hong Kong, ³Hospital Authority, Hong Kong

Seroprevalence survey is the most practical method for accurately estimating infection attack rate (IAR) in an epidemic such as influenza. These studies typically entail selecting an arbitrary titer threshold for seropositivity (e.g. microneutralization [MN] 1:40) and assuming the probability of seropositivity given infection (infection-seropositivity probability, ISP) is 100% or similar to that among clinical cases. We hypothesize that such conventions are not necessarily robust because different thresholds may result in different IAR estimates and serologic responses of clinical cases may not be representative. To illustrate our hypothesis, we used an age-structured transmission model to fully characterize the transmission dynamics and seroprevalence rises of 2009 influenza pandemic A/H1N1 (pdmH1N1) during its first wave in Hong Kong. We estimated that while 99% of pdmH1N1 infections became MN1:20 seropositive, only 72%, 62%, 58% and 34% of infections among age 3-12, 13-19, 20-29, 30-59 became MN1:40 seropositive, which was much lower than the 90%-100% observed among clinical cases. The fitted model was consistent with prevailing consensus on pdmH1N1 transmission characteristics (e.g. initial reproductive number of 1.28 and mean generation time of 2.4 days which were within the consensus range), hence our ISP estimates were consistent with the transmission dynamics and temporal buildup of population-level immunity. IAR estimates in influenza seroprevalence studies are sensitive to seropositivity thresholds and ISP adjustments which in current practice are mostly chosen based on conventions instead of systematic criteria. Our results thus highlighted the need for reexamining conventional practice to develop standards for analyzing influenza serologic data (e.g. real-time assessment of bias in ISP adjustments by evaluating the consistency of IAR across multiple thresholds and with mixture models), especially in the context of pandemics when robustness and comparability of IAR estimates are most needed for informing situational awareness and risk assessment. The same principles are broadly applicable for seroprevalence studies of other infectious disease outbreaks.

Ref. No.: 10090272

P111-Ab0093

Effectiveness of School Closures for Pandemic Influenza

Joseph Wu¹, Daihai He²

¹The University of Hong Kong, Hong Kong, ²The Hong Kong Polytechnic University, Hong Kong

Large-scale antiviral intervention is now a major component of influenza pandemic preparedness planning in many countries. The emergence and spread of antiviral resistance (AVR) can substantially attenuate the effectiveness of large-scale antiviral intervention (e.g. targeted prophylaxis) and worsen the prognosis of severe cases (because antivirals will not be efficacious for cases infected with resistant strains). Reliable and timely estimates of the transmissibility of resistant strains is a public health priority once AVR is detected during an influenza pandemic.

Ref. No.: HK-09-04-01

P112-Ab0095

Direct Identification and Quantification of Host and Viral Transcriptomes after Influenza Infection Using the Next Generation Ultra-High Throughput DNA sequencer

Na Zhang¹, Yun-Juan Bao¹, Amy Tong¹, Malik Peiris², Si Lok¹, Man-Yan Lee²

¹Centre for Genomic Sciences, The University of Hong Kong, Hong Kong, ²Centre of Influenza Research, School of Public Health, The University of Hong Kong, Hong Kong

Introduction: Highly pathogenic avian influenza H5N1 virus causes lethal disease in humans. This virus can trigger a rapidly progressive viral pneumonia leading to acute respiratory distress syndrome. Studies from clinical, in vivo and in vitro data suggest a role of virus induced cytokine dysregulation in contributing to the pathogenesis of human H5N1 disease, however, the precise mechanisms by which the H5N1 virus elicits the differential and unique host responses are still not well understood.

Methods: To better understand the molecular events at the earliest time points, we used RNA-Seq to quantify and compare the host and viral transcriptomes induced by highly pathogenic H5N1 (A/Vietnam/3212/04) or low virulent H1N1 (A/Hong Kong/54/98) influenza viruses in human monocyte-derived macrophages at different post infection time.

Results and Conclusions: Our data revealed that our samples contained a variable mix of two macrophage populations corresponding to the M1 (classically activated) and M2 (alternatively activated) macrophage subtypes, a distinction not possible with previous microarray studies. When this confounding variable is considered in our statistical model, a clear set of dysregulated genes and pathways emerges at 6 hour post infection specifically in H5N1-infected macrophages, but not with H1N1 infection. Furthermore, we mapped reads comprise annotated known miRNA and found a distinct cellular miRNA expression patterns in response to influenza virus infection. We analyzed a set of potential miRNA target genes based on an inversely correlated expression pattern between the target mRNA and miRNAs and highlighted that innate immunity pathways particularly RIG-I like receptor signaling is significantly enriched in response to infection. In addition to known miRNAs, we have also identified some novel human miRNA species which have not been reported previously, while no miRNA was found to be encoded by influenza viruses.

Ref. No.: 08070532